Long-term eradication of extranodal natural killer/T-cell lymphoma, nasal type, by induced pluripotent stem cell-derived Epstein-Barr virus-specific rejuvenated T cells in vivo.

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Public Summary:
Functionally rejuvenated induced pluripotent stem cell-derived antigen-specific cytotoxic T lymphocytes (rejCTLs) are being developed as an anti-cancer immunotherapy. Here, we demonstrate prolonged and robust eradication of Epstein-Barr virus-mediated nasal-type lymphoma using rejCTLs. These results suggest that long-term persistent rejCTLs can contribute to a continuous anti-tumor effect and offer an effective salvage therapy for relapsed and refractory nasal type lymphoma.

Scientific Abstract:
Functionally rejuvenated induced pluripotent stem cell (iPSC)-derived antigen-specific cytotoxic T lymphocytes (CTL) are expected to be a potent immunotherapy for tumors. When L-asparaginase-containing standard chemotherapy fails in extranodal natural killer/T-cell lymphoma, nasal type (ENKL), no effective salvage therapy exists. The clinical course then is miserable. We demonstrate prolonged and robust eradication of ENKL in vivo by Epstein-Barr virus-specific iPSC-derived antigen-specific CTL, with iPSC-derived antigen-specific CTL persisting as central memory T cells in the mouse spleen for at least six months. The anti-tumor response is so strong that any concomitant effect of the programmed cell death 1 (PD-1) blockade is unclear. These results suggest that long-term persistent Epstein-Barr virus-specific iPSC-derived antigen-specific CTL contribute to a continuous anti-tumor effect and offer an effective salvage therapy for relapsed and refractory ENKL.